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Modulation of Methylephedrine HCl Release in Orally Administered, Colon-Specific Pellets

H. H. Lin, H. M. Yu and L. R. Hsu

Department of Pharmacy,
Chia-Nan University of Pharmacy and Science,
Tainan, Taiwan 71710, R.O.C.

ABSTRACT

A multiple unit system such as pellets of chitosan-SLS coacervates has been investigated for colon-specific delivery using Methylephedrine HCl as a model drug. The drug release experiments were carried out in vitro under different conditions to simulate the pH to be encountered during intestinal transit to the colon. The results show the kinetic behavior was controlled by diffusion but not degradation. The addition of chitosan hydrogel solution instead of water as a binding agent during the granulation seemed to yield slower drug release in pH 1.2 medium. The effect of copolymer on retarding release of the drug from pellets in a 0.1N HCl (pH 1.2) conformed to the following order: non-ionic polymer (ex: PVA) > anionic polymer > cationic ploymer. The formation of an insoluble ion complex by chitosan and opposite charge ion was increased the percentage of drug and chitosan release from pH1.2 to pH 6.8 buffer medium. The properties of the composite pellets are suitable for colon targeting. The differential thermal analysis was shown that there is no significant interaction can be observed among the excipients of pellets except adding sodium lauryl sulfate to form coacervate.

Key words: Methylephedrine HCl, Chitosan, Colon-specific delivery, Pellet.

INTRODUCTION

Obesity is one of the pathologies with ever-increasing prevalence in modern societies. Drug that act through noradrenergic and serotonergic mechanisms have historically served as the mainstays of pharmacologic treatments for obesity.[1] Methylephedrine HCl has adrenoceptor agonist activity[2], and may be possibly serve a therapeutic role. Methylephedrine HCl is readily soluble in water, whereas it is subject to gut wall metabolism and thought to be absorbed erratically[3]. It is well known that no digestive enzymes are secreted in the colon[4]. With respect to delivery of drug to the colon to avoid intestinal wall metabolism, natural polysaccharides are now extensively used for development of solid dosage forms as colon-specific drug carrier systems[5-7]. Chitosan is one of the natural polysaccharides[8], which was prepared from chitin of crabs and lobsters by N-deacetylation with alkali. It has recently been used in

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口服投藥後具結腸專一性之圓粒其鹽酸甲基麻黃素釋放之調節

林恆弘　游慧美　許立人

嘉南藥理科技大學藥學系

摘　要

本研究使用一種由幾丁質與sodium lauryl sulfate之共聚物所形成的多個體圓粒系統，供作爲模式藥物鹽酸甲基麻黃素具結腸專一性的藥物輸移。其藥物釋離試驗是模擬小腸至結腸的pH值，結果所獲得的動力學性質是由擴散而非崩解來控制。於造粒時添加幾丁質親水膠體溶液取代純水作爲黏合劑，則可在pH1.2的酸性媒液中產生較慢的藥物釋放速率；共聚物對延遲藥物自圓粒釋離的影響其大小順序依序爲:非離子型聚合物>陰離子型聚合物>陽離子型聚合物，利用幾丁質與相反電荷離子形成不溶性的離子複合物，則隨著酸鹼值由pH1.2至pH6.8其藥物與幾丁質的釋出百分比亦隨之增加，此圓粒之特性適足以作爲結腸標的的運用，而熱分析的結果顯示，除添加sodium lauryl sulfate之共聚物外，其餘的賦形劑間並未有明顯的交互作用。

關鍵字：鹽酸甲基麻黃素、幾丁質、結腸專一性輸移、圓粒